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Collagen Application Versus Manual Compression: A Prospective Randomized Trial for Arterial Puncture Site Closure After Coronary Angioplasty

EDOARDO CAMENZIND, MD,* MARIANNE GROSSHOLZ, MD, PHILIP URBAN, MD, PIERRE-ANDRÉ DORSAZ, PHD, DOMINIQUE DIDIER, MD, BERNHARD MEIER, MD, FACC

Geneva, Switzerland

Objectives. **This study evaluated the safety and efficacy of a newly developed puncture-sealing device consisting of subcutaneous bovine collagen application designed to facilitate local hemostasis after coronary angioplasty.**

Background. **The most common local hemostatic procedure after coronary angioplasty consists of heparin discontinuation and delayed sheath removal followed by mechanical compression at the puncture site.**

Methods. **Between December 1991 and February 1993, 124 patients undergoing coronary angioplasty with either a 6F guiding catheter followed by a heparin infusion for >12 h or a 7F or 8F guiding catheter with optional heparin infusion were prospectively randomized to either delayed sheath removal followed by manual compression (n = 62) or sheath removal immediately after angioplasty combined with bovine collagen application for puncture site closure (n = 62). Half of the collagen plugs were delivered using measured and half using estimated skin–artery distance. Clinical and duplex sonographic evaluations of the puncture site were performed 24 h later.**

Results. **No significant difference in the incidence of local hematomas was observed. Major complications were false aneurysm, venous thrombosis and arterial occlusion. The incidence of false aneurysm was the same in both groups (4 [7%] of 62). Venous thrombosis (2%) and arterial occlusion (2%) were each recorded in one patient, both in the collagen application group.**

Conclusions. **Sheath removal and collagen application with this new vascular hemostasis device used directly after coronary angioplasty are not superior to delayed sheath removal after heparin discontinuation followed by mechanical compression. Arterial collagen sealing with this device in its current form is associated with a small but worrisome risk of arterial occlusion.**

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Reported local complication rates after percutaneous femoral artery puncture vary depending on the type of intervention, the anticoagulation regimen and the prospective or retrospective nature of the evaluation. In small prospective trials (1–3), minor local complications after coronary angiography, such as local hematomas, ranged from 4% to 26%. In larger retrospective studies (4–9) in which, only major local complications requiring surgery or transfusions were reported, local complication rates after diagnostic coronary angiography were 0.5% to 3.5%. These rates do not appear to be higher after angioplasty (6–8,10–13). However, with the advent of more aggressive anticoagulation regimens, such as those currently used after stent implantation, local complication rates have increased to ≤8% (14). This increase has led to the development of new hemostatic devices for arterial puncture site closure. The system used in this study consists of subcutaneously applied collagen for local vascular hemostasis (VasoSeal, Datascope Corporation). Preliminary data (15–17) suggest that it is safe and effective for puncture site closure.

The present randomized study compared the safety and efficacy of two hemostatic procedures for arterial puncture site closure after coronary angioplasty: delayed sheath removal followed by manual compression versus immediate sheath removal and subcutaneous collagen application.

Methods

Study design. One hundred twenty-four patients undergoing percutaneous transluminal coronary angioplasty were prospectively randomized to either delayed sheath removal followed by manual compression (manual compression group, n = 62) or immediate sheath removal after coronary angioplasty combined with bovine collagen application for puncture site closure (collagen group, n = 62). Inclusion criteria were 1) coronary angioplasty performed with a 6F guiding catheter and full-dose heparinization for >12 h, or 2) coronary angioplasty with 7F or 8F guiding catheters and optional subsequent heparinization. The distribution of patients according to size of the sheath, anticoagulation regimen after angioplasty and type

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*Present address and address for correspondence: Dr. Edoardo Camenzind, Bd 376 Thoraxcenter, Cardiology Department, P.O. Box 1738, 3000 DR Rotterdam, The Netherlands.

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Table 1. Patient Distribution According to Type of Hemostasis, Postprocedural Heparin Regimen and Sheath Size

	Manual Compression Group (n = 62)		Collagen Group (n = 62)	
Sheath Size	Total Group (n = 62)	Heparin >12 h (n = 24)	Total Group (n = 62)	Heparin >12 h (n = 25)
6F	6 (10%)	5 (21%)*	8 (13%)	6 (24%)†
7F	51 (82%)	16 (67%)	44 (71%)	14 (56%)
8F	5 (8%)	3 (12%)	10 (16%)	5 (20%)

In one (*) and two (†) patients, respectively, heparin perfusion was stopped by the operator ≤12 h after reviewing coronary angioplasty film. Data are expressed as number (%) of patients. There were no significant differences among groups.

Table 2. Patient Characteristics and Procedural Aspects at Puncture Site

	Manual Compression Group (n = 62)	Collagen Group (n = 62)
Male gender	53 (85%)	50 (81%)
Age (yr)	60 ± 11	59 ± 12
Body mass index (ratio of body weight [kg] to height [cm])	0.46 ± 0.06	0.44 ± 0.05
Blood pressure (mm Hg) at end of PTCA		
Systolic	122 ± 21	120 ± 18
Diastolic	76 ± 11	76 ± 9
Thrombocyte (10^3/μl)	260 ± 56	273 ± 75
Prothrombin time (%)	86.0 ± 16.3	87.7 ± 16.6
Activated partial thromboplastin time (s)	36.0 ± 18.8	36.8 ± 17.2
Fibrinogen (mg/dl)	304 ± 74	336 ± 135
Direct arterial puncture	59 (95%)	60 (97%)
Duration of procedure (min)	108 ± 32	111 ± 36

Data presented are number (%) of patients or mean value ± SD. There was no statistical difference between the two groups. PTCA = coronary angioplasty.

of hemostasis are summarized in Table 1. Of the 49 patients receiving full-dose heparinization, heparin was continued for >24 h in 4 patients (manual compression group 1, collagen group 3) because of stent implantation. Exclusion criteria were 1) preexisting local hematoma, and 2) known allergy to collagen products.

Patients. Patient characteristics, coagulation variables, facility of arterial access, duration of procedure and drug regimen before, during and after coronary angioplasty are reported in Tables 2 and 3. No significant differences between groups were observed. All patients not pretreated with aspirin received an intravenous bolus dose of 250 to 500 mg of aspirin during the procedure. Heparin in a bolus dose of 10,000 to 20,000 IU (as selected by the operator) was administered during angioplasty; ongoing intravenous heparin treatment was given after angioplasty. Urokinase administration did not differ significantly between groups.

Puncture technique. The common femoral artery was punctured 1 to 2 cm below the inguinal fold or at inguinal fold level in obese patients. The arterial puncture was performed by modified Seldinger technique using a beveled thin-walled 18-gauge needle with sharp cutting edge (Homedica-Hollenstein, Cham, Switzerland) with continuous aspiration. A 145-cm long 0.035-in. (0.089-cm) guide wire was then threaded through the iliac artery up to the abdominal aorta before the needle was removed. Intravascular femoral sheaths, 6F to 8F (Cordis, Roden, The Netherlands), were used routinely.

Hemostatic device and physician experience. The recently developed hemostatic device, VasoSeal, has two main elements: 1) a local, subcutaneously applied hemostatic collagen plug, and 2) an applicator system. The collagen is isolated after mechanical and chemical elaboration of bovine achilles tendon. Two 80-mg plugs of purified and sterile collagen are applied subcutaneously directly over the arterial puncture site.

The application system consists of a blunt-tipped dilator, an 11.5F sheath and two collagen-loaded cartridges (Fig. 1). The recommended placement procedure consists of two sequential steps: 1) determination of the skin–artery distance, and 2) actual positioning of the plugs (Fig. 2). In step 1, at the beginning of the catheterization procedure, the needle is clamped at skin level after the artery is punctured, and blood reflow is obtained through the needle bore (Fig. 2, top). This procedure makes it possible to estimate the skin–artery distance and choose the appropriate kit for the subcutaneous depth of the artery (seven color-coded kits, ranging from 3.5 to 7 cm, are available). This is the procedure recommended by the manufacturer and was applied in 31 (50%) of the patients in the collagen group. In the other 31 patients in this group, the skin–artery distance was estimated while the blunt-tipped dilator was introduced over the wire and advanced down to the anterior arterial wall. In step 2, at the end of angioplasty, the collagen is delivered through the applicator system directly over the arterial puncture site (Fig. 2, bottom). The system is designed to seal arterial puncture holes associated with the use of sheaths up to 8F in diameter.

Throughout the study only two operators (B.M. and P.U., each working alone) used the collagen sealing device. The first plug was used at our institution in June 1991, and both operators had placed ~20 plugs before the prospective randomized evaluation was begun.

Hemostatic procedure. In the manual compression group, arterial sheath removal was delayed 4 to 6 h after coronary angioplasty or heparin discontinuation. Manual compression was applied for 15 to 30 min until local hemostasis was achieved. In the collagen group, local hemostasis was performed by local collagen application with immediate sheath removal in the catheterization laboratory followed by a 3- to 5-min period of manual compression. No heparin reversal was used. If immediate hemostasis was not achieved by local collagen application, an air cushion compression device (Femostop, Radi Medical Systems, Uppsala, Sweden) was positioned over the puncture site. An inflation pressure of 50 to 100 mm Hg was continuously maintained for up to 6 h. Both

Table 3. Patient Distribution According to Drug Regimen Before, During and After Coronary Angioplasty and Type of Hemostasis

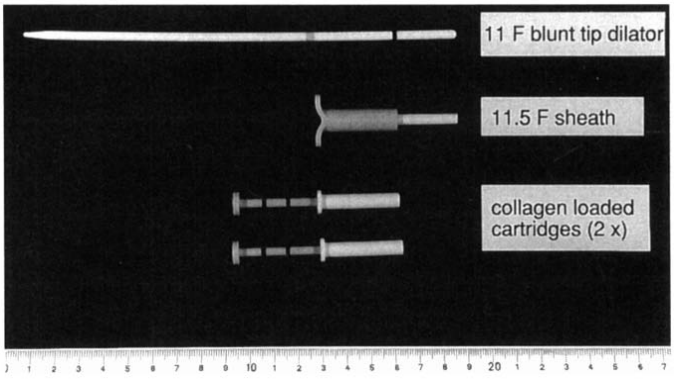
	Before/During PTCA				After PTCA			
	Manual Compression Group (n = 62)		Collagen Group (n = 62)		Manual Compression Group (n = 62)		Collagen Group (n = 62)	
	No.	Dose	No.	Dose	No.	Dose	No.	Dose
Oral								
Coumadin (mg)	3	1.7 ± 0.6	2	2	7	3.4 ± 1.5	4	3 ± 1
Dipyridamole (mg)	2	188 ± 53	1	225	7	204 ± 37	2	188 ± 53
						$p < 0.05$		
Oral or intravenous aspirin (mg)	62	182 ± 139	62	149 ± 126	51	114 ± 48	58	112 ± 59
Intravenous heparin (IU/h or IU)	62	19,745 ± 4,283	62	19,842 ± 4,064	24	1,051 ± 208	25	1,109 ± 144
Intravenous or intracoronary urokinase (10^6 IU)	4	1	9	0.9 ± 0.4	—	—	—	—

Data presented are number of patients or mean value ± SD. PTCA = coronary angioplasty.

groups were treated with a pressure dressing (rolled gauze and elastic bandage) for >6 h and bed rest for >12 h.

Definitions and evaluation criteria. Evaluation criteria included the immediate effect of bovine collagen application on local hemostasis. Immediate hemostasis was defined as complete hemostasis after collagen application without conventional compression. After 24 h, hematoma size, arterial bruit and peripheral pulse were evaluated clinically. A hematoma was defined as a palpable blood collection and assessed clinically. Hematomas were classified by their maximal diameter as absent, <10 cm, 10 to 20 cm or >20 cm. Duplex sonography (Akcuson model 128, 7.5- and 5-MHz probe) of the puncture site was performed after 24 h to evaluate vascular complications. A standard reporting technique was used evaluating 1) the morphology of perivascular structures (echographic imaging assisted by color-coded Doppler signal for vessel location), and 2) arterial and venous flow and flow pattern in suspected false aneurysms and arteriovenous fistulas (pulsed and continuous Doppler analysis). A pseudoaneurysm was defined as a cavity linked to the arterial lumen with turbulent color flow pattern and biphasic flow specter on pulsed Doppler analysis. Two physicians interpreted the ultrasound examinations without knowledge of treatment assignment.

Figure 1. VasoSeal applicator system.



Statistics. Baseline characteristics were expressed as mean value ± SD when appropriate. Continuous variables were compared with the Mann-Whitney *U* test for unpaired groups. Discrete variables were compared with the chi-square test. Differences with a p value < 0.05 were considered statistically significant.

Results

Immediate hemostasis. Immediate hemostasis after bovine collagen application for puncture site sealing was achieved in 58 (94%) of 62 cases whether or not previous skin–artery measurement had been performed. In four patients immediate hemostasis was not achieved, and prolonged mechanical compression (Femostop) had to be used. Immediate hemostasis after manual compression was not an issue as such because it had to be achieved before application of the pressure dressing.

Results after 24 h. The distribution of hematomas after 24 h is depicted in Figure 3. No significant difference in incidence and size could be observed between manual compression and collagen application. Hematomas were observed in 22 (36%) of 62 patients in the manual compression group and in 30 (48%) of 62 in the collagen group. Very large hematomas (>20 cm) were found only in the collagen group (0 vs. 4 [7%]). However, no hematoma required transfusions or surgery. Within the collagen group, previous skin–artery measurement did not influence the incidence of hematoma formation. Major complications assessed clinically or by duplex sonography are summarized in Table 4. The characteristics of the patients who had a major complication are summarized in Table 5. The incidence of false aneurysm was the same in both groups; however, venous thrombosis and arterial occlusion were observed in one patient each after collagen application.

Venous thrombosis (Patient 55). A 34-year old hypercholesterolemic manual worker presented with clinically apparent venous thrombosis 3 h after subcutaneous application of the collagen plug despite ongoing full-dose anticoagulation for emergency stent implantation. Puncture of the artery at the beginning of the procedure had been easy, and the vein had

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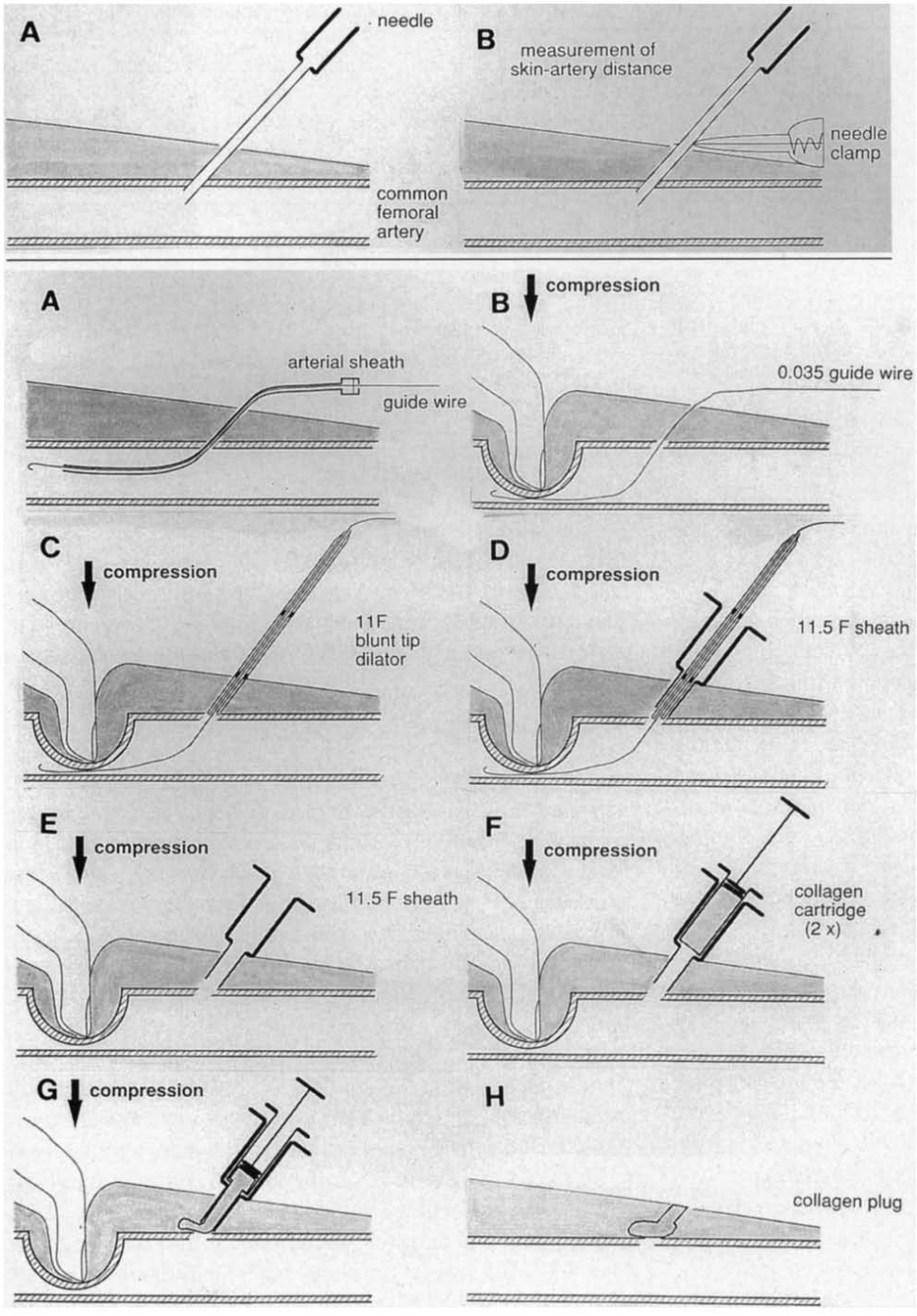

Figure 2. Technique for application. **Top: A,** At the beginning of the procedure, the artery is punctured with an 18-gauge beveled needle. **B,** When blood reflows through the bore, the skin–artery distance is measured by clamping the needle at skin level. **Bottom: A,** At the end of the procedure, a 0.035-in. (0.089-cm) guide wire is inserted through the arterial sheath. **B,** The sheath is removed, leaving the guide wire within the artery. **C,** A blunt-tipped dilator is introduced and advanced down to the anterior arterial wall. **D,** An 11.5F sheath is inserted over the dilator. **E,** The guide wire and blunt-tipped dilator are removed. **F,** The collagen-loaded cartridge is inserted into the sheath. **G,** The collagen is applied. **H,** The arterial puncture site is sealed by collagen.

not been punctured. After collagen application with the estimation technique, hemostasis was not immediately complete, and an air cushion compression belt was applied for 3 h. At duplex ultrasound examination, venous thrombosis extended from the superficial femoral vein to the external and common femoral vein. The collagen plug was visualized between the common femoral artery and vein. Phlebography revealed a long occlusion of both internal and external femoral veins.

Arterial occlusion (Patient 106). A 45-year old office clerk, hypercholesterolemic and current smoker, developed an arterial occlusion late after collagen application. After previous easy arterial puncture and an uncomplicated procedure, the 7F sheath was withdrawn, and collagen plugs were implanted after previous skin–artery measurement. Immediate hemostasis was successful. After >12 h the patient was free of symptoms. There was no local hematoma, and peripheral pulses were easily palpable. Eighteen hours after the procedure, a bicycle stress test was performed. During the test the patient reported sharp pain in the right leg. Clinically the signs of an acute arterial occlusion were evident as pallor, thermal gradient distal to the knee and absence of peripheral pulses. Angiography revealed occlusion of the right common femoral artery at

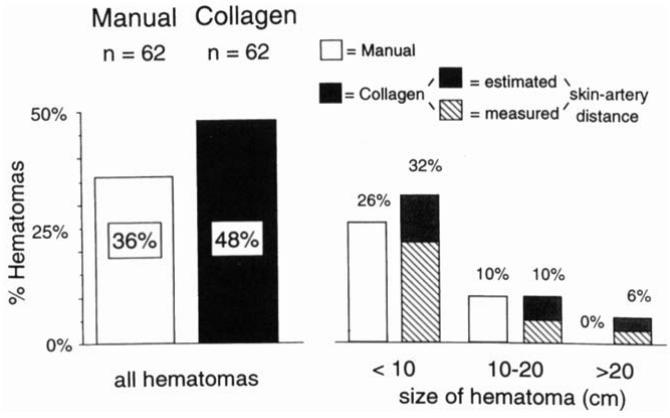

Figure 3. Incidence of hematomas 24 h after coronary angioplasty. No significant difference was observed between delayed sheath removal followed by manual compression or immediate sheath removal and collagen application. Within the collagen group, previous skin–artery measurement did not influence the final incidence of hematomas.

puncture site level. Intraoperatively the collagen plug was found to be dislocated intraarterially and appeared as a gelatinous mass. Surgical removal was performed with a Fogarty 4 catheter, and the arteriotomy was closed by venous patch.

Discussion

Background and objectives. Several large retrospective studies (6–8,13) have shown that complication rates at the puncture site are not higher after coronary angioplasty than after coronary angiography and range between 0.5% and 3.5%. An increased risk of local complications after coronary angioplasty has been reported (18) to be associated with advanced age, female gender, thrombolytic therapy and postprocedural anticoagulation.

With the advent of more aggressive and sustained postprocedural anticoagulation regimens, attempts have been made to decrease local complications by 1) miniaturization of instruments (19–21); 2) use of different arterial puncture sites, such as transbrachial sites (22–24); and 3) development of new devices for local hemostasis.

VasoSeal, a new hemostatic device, consists of a subcutaneously implantable collagen plug for vascular closure of the arterial puncture site (Fig. 1). Historically the first report of the clinical use of collagen was made in 1960 by Neuner (25) in the odontologic field. Since then, its hemostatic properties have been applied in abdominal and vascular surgery for >20 years (26,27). The procoagulative properties are primarily linked to platelet adhesion and activation (28,29) and vary according to the chemical and mechanical properties of the collagen used (28,30,31). Anticoagulation and antiaggregation therapy seem not to affect the hemostatic properties of collagen (32). Bovine collagen is biodegradable and was reabsorbed within 4 weeks in animal experiments (33,34). No pyrogenic or allergenic reaction has been described in animal (35) or human (15,17) trials.

Table 4. Major Complications Assessed Clinically and by Duplex Sonography 24 h After Hemostasis

	Manual Compression Group (n = 62)	Collagen Group (n = 62)	
		Measured (n = 31)	Estimated (n = 31)
False aneurysm	4 (7%)	2 (3%)	2 (3%)
Venous thrombosis	0	0	1 (2%)
Arterial occlusion	0	1 (2%)	0

Data presented are number (%) of patients in hemostasis group (n = 62). There was no statistical difference among groups.

The goal of this randomized trial was to compare the efficacy and safety of arterial puncture site closure by conventional technique (delayed sheath removal 4 to 6 h after coronary angioplasty or after discontinuation of heparin and manual compression) or by collagen application (immediate sheath removal at the end of the procedure and local, subcutaneous collagen plug application).

Incidence of complications. In our prospective, clinically and duplex sonographically controlled evaluation, the total local complication rate after coronary angioplasty was 42% (26 of 62) in the manual compression group and 58% (36 of 62) in the collagen group (p = NS). Minor complications (hematomas not needing transfusions) were present in 35% (22 of 62) in the manual compression group and in 48% (30 of 62) in the collagen group (p = NS). This complication rate may appear excessively high. However, a hypothetic retrospective evaluation of this same series would have resulted in a total complication rate of 1.6% in both the manual compression group and the collagen group (one venous thrombosis vs. one arterial occlusion) because neither hematomas not requiring transfusions nor subclinical false aneurysms are reported in retrospective analysis. This complication rate is of the same magnitude as that previously reported (6–8,10–13) but does not reflect actual events at the patient's puncture site.

In our study the incidence of false aneurysm was the same in both the manual compression and collagen groups (4 [7%] vs. 4 [7%]). All eight pseudoaneurysms (Table 5) were detected by duplex sonography but were not suspected by clinical examination because of absence of a pulsating mass or an arterial bruit. Therefore, they can be considered subclinical false aneurysms. No patient needed surgery. All could be treated by local external compression with the duplex sonographic probe. This technique allowed a localized compression directly on the neck of the false aneurysm (36).

Thrombosis of the superficial femoral vein (Table 5) occurred in 1 patient despite ongoing full-dose anticoagulation. A potential explanation for the venous thrombosis was venous stasis induced by the synergistic action of mechanical external compression, local hematoma (mild <10 cm) and collagen plug position between vein and artery.

The rate of arterial occlusion after collagen plug application has ranged from 0% to 1% in reported series (17,37) and was 2% in our series. This small but worrisome risk of distal

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Table 5. Characteristics of the 10 Male Patients With a Major Complication

	Manual Compression Group				Collagen Group					
	False Aneurysm				False Aneurysm				Venous Thrombosis	Arterial Occlusion
Patient no.	12	52	96	120	9	25	35	110	55	106
Age (yr)	68	75	54	74	54	56	53	49	34	45
Body mass index (ratio of body weight [kg] to height [cm])	0.51	0.43	0.39	0.39	0.38	0.39	0.40	0.44	0.43	0.44
Puncture type (1 or >1)*	1	1	1	1	1	1	1	1	1	1
Sheath size	7F	8F	7F	6F	6F	8F	8F	7F	7F	7F
Drug regimen										
Before and during angioplasty										
Oral coumadin (mg)	—	—	—	1	—	—	—	—	—	—
Oral and intravenous aspirin (mg)	250	100	350	250	100	100	—	100	350	100
Intravenous heparin (IU/h + 10^3 IU)	— + 20	— + 30	— + 15	1,042 + 10	1,042 + 20	— + 20	— + 30	— + 20	1,042 + 20	1,250 + 15
Intravenous or intracoronary urokinase (10^3 IU)	—	—	1	—	—	—	—	—	—	—
After angioplasty										
Oral										
Aspirin (mg)	100	100	100	—	100	100	100	100	100	100
Coumadin (mg)	—	—	—	2	—	—	—	—	—	—
Dipyridamole (mg)	—	225	225	—	—	—	—	150	—	—
Intravenous heparin (IU/h)	—	1,250	1,042	1,042	1,042	—	1,042	1,042	1,042	—

*1 = direct, easy; >1 = multiple, difficult.

embolization of collagen (37) or acute arterial occlusion at the level of the puncture site might be related to a learning curve.

Potential factors influencing results. *1) Learning curve.* The rate of hematoma in the 62 patients in the collagen group was 55% (17 of 31) in those treated early (Patients 1 to 31) in our experience versus 42% (13 of 31) in those treated late (Patients 32 to 62) (p = NS). Important hematoma (>20 cm) and false aneurysm were equally distributed in the early and late treatment groups (2 of 31 vs. 2 of 31 and 2 of 31 vs. 2 of 31). Venous thrombosis occurred after the 27th and arterial occlusion after the 52nd plug insertion. These data make a masked learning curve phenomenon unlikely.

2) Operator. Hematoma incidence was 50% (14 of 28) with operator B.M. versus 47% (16 of 34) with operator P.U. (p = NS) and important hematoma and false aneurysm were similarly distributed: 2 of 28 versus 2 of 34, and 2 of 28 versus 2 of 34, respectively. Venous thrombosis and arterial occlusion were also evenly distributed (1 of 28 vs. 1 of 34). These data make an operator-biased result unlikely.

3) Mode of application. Precise application of the collagen plug, with slight pressure over the arterial puncture site, is of particular importance for hemostatic efficacy. However, it also increases the likelihood of the most feared complication, arterial occlusion. Two application methods were tested in our series: 1) that recommended by the manufacturer, with previous skin–artery depth measurement, and 2) that in which arterial depth is estimated by careful advancement of the blunt tip dilator over the wire until the elastic recoil of the anterior arterial wall is felt. The incidence of total complications did not differ significantly between the two application methods. Thus, the type of application method does not seem to influence the incidence of minor or major complications (Table 4), and previous skin–artery measurement does not reliably exclude dislocation of collagen into the arterial lumen.

Although these results can be interpreted as initial experience, the relatively simple design of the device, the absence of a learning curve and the lack of an operator bias or application method bias make it unlikely that a substantial improvement of efficacy will occur over time.

Potential disadvantages of arterial collagen sealing. There are several additional disadvantages of this device. 1) It must be used directly after the angiographic or angioplastic procedure. Delayed application is not recommended because of the potential risk of local infection. However, one study (38) undertook delayed placement without reported infections. 2) Repuncture of the same artery within 1 month is not recommended, because biodegradation and reabsorption of the collagen must be allowed for. Early repuncturing could carry a risk of potential intraluminal dislocation of the collagen, inducing either local thrombosis or embolization in the periphery. 3) The late proliferative reaction induced by collagen, seen in an animal model (33), could lead to subcutaneous scar formation and make future arterial access difficult. This concern is heightened by an anticipated 30% risk of a second intervention within 6 months (39). 4) The additional cost of the device must also be considered.

Potential advantages of arterial collagen sealing. The potential major advantage of this device is to allow immediate sheath removal and immediate hemostasis, even in patients with a high level of anticoagulation (in a subset of seven

patients, measured activated partial thromboplastin time and prothrombin time were >200 s and 15 ± 10%, respectively, at the moment of collagen plug insertion). This is time-saving and may avoid the infrequent local complications related to leaving intraarterial sheaths in place for prolonged periods (40).

Early mobilization has been suggested by some investigators (15,17,38,41) as one of the major advantages of collagen puncture site sealing by VasoSeal. However, none of these studies had a control group for this issue. Of the two reported prospective randomized studies comparing collagen application with mechanical compression, the first (41) mobilized patients with collagen after 6 h and kept patients after mechanical compression at rest for >12 h and the second (38) collected the data concerning this issue retrospectively. In the present series consisting of a mixed in-hospital patient group with postinfarction coronary angioplasty, stent implantations and elective angioplasty, time to discharge is unlikely to have been influenced by puncture site care. Irrespective of the clinical indication for angioplasty, hospital stay did not differ significantly between groups (manual compression group 5.7 ± 5.3 days vs. collagen group 5.2 ± 4.1 days). These data indicate that the time to mobilization saved by collagen application still needs further evaluation.

Comparison with previously reported data. Some earlier studies evaluating the VasoSeal system (17,41) did not take into account the type of intervention and the anticoagulation regimen used. Therefore, these results have to be interpreted with caution. The following comparison focuses on previous studies evaluating collagen sealing (VasoSeal) in patients with a high level of anticoagulation and is limited to major complications (surgery, blood transfusion, false aneurysm or venous thrombosis).

In patients receiving postprocedural heparin for >24 h, the data are scarce. In an observational study (16) of 10 such patients (all with stents), immediate hemostasis after sheath removal was achieved in 9 of the 10. At 24 h one patient (10%) had developed a clinically important hematoma requiring transfusions. However, in that preliminary report 8 of the 10 patients had a combined hemostatic procedure of collagen and mechanical compression. Our observations in a similar subgroup of patients with postprocedural heparin for >24 h (three patients with stent implantation in the collagen group) revealed at 24 h one false aneurysm (Patient 110 in Table 5) and one venous thrombosis (Patient 55 in Table 5), a complication not attributable to the sustained anticoagulation regimen. However, these data are anecdotal and do not permit a conclusive statement.

A recent randomized study (38) evaluated prospectively collagen sealing versus conventional hemostatic technique (mechanical compression) for arterial puncture site closure 1) after coronary angiography, 2) after coronary angioplasty with previous discontinuation of heparin, and 3) directly after coronary angioplasty. This latter subgroup of 85 patients (high level of anticoagulation at the moment of plug insertion, no postprocedural heparin treatment) presents an opportunity for comparison with the current series. In the previous study, the incidence of major complications was 7 (8%) of 85 compared with 9 (4%) of 134 in the control group with conventional hemostatic technique (mechanical after heparin discontinuation). In our series, the major complication rates were fairly similar: 6 (10%) of 62 in the collagen group and 4 (7%) of 62 in the manual compression group. The higher incidence of complications in our series can be explained in part by 1) the detection of clinically unsuspected false aneurysms (duplex sonographic screening versus clinical evaluation), and 2) the use in some patients of a postprocedural anticoagulation regimen after collagen sealing. Analysis of our collagen group patients according to postprocedural heparin regimen revealed a major complication rate of 16% (4 of 25) in the subgroup receiving intravenous heparin for >12 h versus 5% (2 of 37) in the group in which heparin was discontinued (p = NS). This same analysis applied to the manual compression group showed a major complication rate of 13% (3 of 24) in the continued heparin subgroup versus 3% (1 of 38) in the discontinued heparin subgroup (p = NS). This analysis suggests a trend toward an increased incidence of major complications in patients with maintained postprocedural anticoagulation. Analysis of the entire study group (collagen plus manual compression group) according to postprocedural heparin regimen confirmed previous reports (18) of a significantly higher risk of local complication (7 of 49 with continued heparin vs. 3 of 75 with discontinued heparin, p = 0.05) in the subgroup receiving intravenous heparin for >12 h. Collagen application did not decrease the incidence of complications observed with manual compression (4 of 25 vs. 3 of 24) in the subset of patients receiving heparin.

Clinical implications. The indications for the use of this subcutaneous hemostatic device in its current form must be derived from its established benefits and potential risks. Its recognized benefit is its ability to provide immediate hemostasis even in patients with a high levels of anticoagulation. In view of the most serious potential risk—arterial occlusion—the use of this device should be limited to patients requiring uninterrupted full-dose anticoagulation therapy (e.g., stent implantation). This indication is based on the hypothesis that the risk of potential arterial occlusion and the possible long-term local fibrotic scarring are less worrisome than the potential consequences of a temporarily diminished anticoagulation regimen. However, our data suggest that this subcutaneous hemostatic device in its current form needs further improvement to achieve reliable sustained hemostasis in this subgroup of patients. At present, this system appears to require the use of an additional device such as a mechanical compressor in patients with a prolonged postprocedural anticoagulation regimen.

Conclusions. Subcutaneous application of collagen for arterial puncture site closure has opened the way to immediate sheath removal after coronary angioplasty in patients with a high level of anticoagulation. However, our data and previous reports suggest that the VasoSeal system does not currently possess adequate efficacy and safety to warrant routine use after angioplasty. Its potential benefits when combined with mechanical compression

and applied to patients requiring sustained anticoagulation need further randomized investigation.

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